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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/692,072	10/22/2003	David Botstein	GNE.2930R1C10C1	8436
20995	7590	04/10/2006		
KNOBBE MARTENS OLSON & BEAR LLP 2040 MAIN STREET FOURTEENTH FLOOR IRVINE, CA 92614			EXAMINER FREDMAN, JEFFREY NORMAN	
			ART UNIT	PAPER NUMBER
			1637	

DATE MAILED: 04/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/692,072	Applicant(s) BOTSTEIN ET AL.	
	Examiner Jeffrey Fredman	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>5/20/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Rejections - 35 USC § 112 – Written Description

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 22-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification, since the claims are not limited to any particular SEQ ID NO, but are open to a nucleic acid that ranges from 95% to 99% identical to SEQ ID NO: 7, without any guidance on conserved portions of the protein structure.

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members, the court in Lilly required “A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. (Lilly at page 1406).” (As a side comment, the genus size here is larger than that at issue in Deuel). Lilly continues to note that in other cases, two chemical compounds in a subgenus were insufficient to describe that genus.

In fact, this genus estimate is actually only a fraction of the total true genus size. Since this estimate does not take into account positional variation (ie, the difference between a sequence that is ACC and CAC) and since this estimate does not incorporate the redundancy of the genetic code (that a single amino acid can be encoded by multiple different nucleic acid sequences), the actual genus size is orders of magnitude greater than 20^{41} .

In the current case, a single species of a single SEQ ID NO is not sufficient to describe at least 20^{41} other sequences for which no description whatsoever is given. These sequences may be of any size or structure, so long as they are 95% identical. There is no expectation in the instant case of insubstantial variation because the functional limitation devolves solely to the ability of the protein to “associated with formation of the growth of lung or colon tumor”. However, this induction is entirely unrelated to the structure of the protein. The function provides absolutely no guidance or information regarding the structure and does not delimit the structure in even the smallest or most miniscule possible way.

The size of the genus is a central issue. If the genus were small, a written description rejection would be less likely, since the examples would be more representative of the genus. Here, where the genus includes 21,990,232,555,520,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000 different members, none of which are disclosed or taught by Applicant, the argument that the demonstrated species is representative is not found persuasive.

Absence of any structure-function relationship

The written description guidelines analysis is based upon the assumption that there will be insubstantial variation, as noted in many of the examples including example 9.

There is no showing or evidence which links structural limitations or requirements to any particular functional limitations. Further, these claims expressly encompass alternately spliced versions of the nucleic acids, allelic variants including insertions and mutations, nucleic acids which encode inactive precursor proteins which have a removable amino terminal end, and only specific nucleic and amino acid sequences have been provided. No written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

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"A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers*, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing *Amgen*). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the nucleic acids as having 95%-99% sequence identity to SEQ ID NO: 7 lacks any specific structure, since it lacks the correlation between structure and function that is at the heart of the caselaw and of the written description guidelines.

It is noted that in *Fiers v. Sugano* (25 USPQ2d, 1601), the Fed. Cir. concluded that

"...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound without identifying the structure function relationship of the compound, so that the compound is claimed solely its nucleic acid sequence related 95%-99% to SEQ ID NO: 7 without any meaningful correlative function to delimit the structure. The correlative function recited, "associated with formation of the growth of lung or colon tumor", does not provide a limitation in

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accordance with the written description guidelines. The guidelines contemplate that a protein that is a conserved member of a known family of proteins, where specific domains of the proteins are known in the prior art to be conserved regarding function, may utilize percent homology language. However, the function is one which serves to delimit the genus being claimed based upon known structures of the protein. That is not the case in the current situation because the function of "associated with formation of the growth of lung or colon tumor" provides no reliable guide to identify members of the genus based upon any structural considerations.

There is no expectation in the instant case of insubstantial variation because the functional limitation devolves solely to the ability of the protein to "associated with formation of the growth of lung or colon tumor". This is not like example 9, where the functional limitation involved a protein which retained adenylate cyclase activity. In the example 9 case, the argument of insubstantial variation was that there was an expectation that stringently hybridizing proteins which retained the specific function of stimulating adenylate cyclase would differ insubstantially. The current claims fails to equate with the written description guidelines because in the guidelines, there is function correlated to the structure. The function in Applicant's claims, however, lack any association with the structure of the protein whatsoever. So consonant with the case law in Lilly, Enzo and the other written description decision of the Federal Circuit, it is clear that the current claims fail to meet the written description requirement because there is no structure function relationship which limits the genus size. The guidelines require more. They require a structure function relationship.

Conclusion

The decisional law in this area has been very consistent. The Federal Circuit in Lilly, Fiers, Rochester and many other cases has determined that the written description issue applies to situations where the definition of the subject matter of the claims fails to provide description commensurate with the genus. The most recent caselaw directly supports this rejection. As the District Court in University of Rochester v. G.D. Searle & Co., Inc. (2003 WL 759719 W.D.N.Y., 2003. March 5, 2003.) noted "In effect, then, the '850 patent claims a method that cannot be practiced until one discovers a compound that was not in the possession of, or known to, the inventors themselves. Putting the claimed method into practice awaited someone actually discovering a necessary component of the invention." This is similar to the current case since the breadth of the current invention claims comprise compounds which were not in the possession of, or known to the inventors. In a genus that is literally unimaginably immense, the specification shows one embodiment.

The claims include a single species which is not representative of the full scope of the genus. The guidelines support the rejection, particularly the requirement of Example 9 for a structure function relationship.

As noted in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), the Federal Circuit concluded that:

"...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

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In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which encode SEQ ID NO 7. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Jeffrey Fredman
Primary Examiner
Art Unit 1637

3/23/06